Supplementary Methods

Testing for pleiotropy using SMR/HEIDI approach

SMR/HEIDI analysis was conducted as described by Zhu et al.[1] HEIDI statistics was calculated as $T_{HEIDI} = \sum_i^m z_{d(i)}^2$, where *m* is the number of SNPs selected for analysis, $z_{d(i)} = {d_i}/{SE_{(d_i)}}$ and $d_i = \beta_{SMR_i} - \beta_{SMR\ (lead\ SNP)}$.

SNP selection was performed as follows:

1) We defined a set of eligible markers within ±250 kb from the lead SNP in the primary GWAS, which had $\chi^2 > 10$ in the primary GWAS, and for which the results were reported in the secondary GWAS;
2) Made empty "target" and "rejected" SNP sets;
3) Selected SNP from the primary GWAS with the lowest *P*;
4) If this SNP had $r^2 > 0.9$ with any SNP in the target SNP set, we added it to the "rejected" set. LD matrix (r^2) was computed with PLINK 1.9 (https://www.cog-genomics.org/plink2) using 1000 Genomes data for 503 European individuals (http://www.internationalgenome.org/data/);
5) Otherwise, it was added to the "target" set;
6) Procedure was repeated from the step 3) until either eligible SNP set was exhausted, or the "target" set had 20 SNPs. If we could not select 3 or more SNPs, no test was performed.

GWAS summary statistics for VVs was obtained from the Gene ATLAS database (I83_GA). Analysis was conducted using Python 3.5 as the main programming language.

REFERENCES:

1. Zhu, Z. et al. Integration of summary data from GWAS and eQTL studies predicts complex trait gene targets. *Nat. Genet.* **48**, 481–7 (2016). doi:10.1038/ng.3538